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Itch Evoked by Electrical Stimulation of the Skin

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Psychophysical experiments were done to test the possibility that a single receptor population signals both itch and pain by generating different patterns of activity for each type of stimulus. Electrical stimulation of hairy skin evoked pruritus in 92% of the subjects tested, and for the majority the pruritus elicited by electrical stimulation felt the same as that provoked by cowhage. The intensity of pruritus increased with the frequency of stimulation with no change in the quality of the sensation from itch to pain. Electrical stimulation of human skin with response patterns obtained from individual cat polymodal nociceptive neurons to pain- and itch-producing stimuli caused no differences in the quality of the evoked pruritic sensations. These results do not support the idea that the same population of primary sensory neurons can produce both itch and pain by changing their pattern of discharge.

The way that itch is signaled to the central nervous system remains a mystery. Historically a popular explanation for the signaling of different sensations was that neurons are nonspecific and transmit sensory qualities by their patterns of activity. For instance, the intensive theory of pain proposes that a high level of activity on neurons that otherwise signal innocuous sensations will produce pain (Goldsheider [1]) [2,3]. A more general theory proposes that the whole spectrum of cutaneous sensations is signaled by differences in the patterns of activity and hence any particular neuron can signal a variety of sensory modalities [4–7]. However the finding that high-frequency, electrical stimulation of large myelinated axons in the peripheral nerves of awake humans consistently evokes painless sensations argues against such models [8,9].

An alternative view, originating with Muller's doctrine of specific nerve energies [10] and expanded by a number of early investigators (von Frey [1]) [11,12], proposes that an individual neuron transmits a specific type of sensory information. The discovery, over a period of years, of cutaneous receptors that respond specifically to heating, cooling [13], light mechanical stimuli [14,15], or noxious stimuli [16–20] has gradually increased support for this hypothesis. The recent findings of Torebjork and Ochoa [21] that electrical stimulation of individual neurons, over a range of frequencies in awake humans, evokes single sensory modalities lends additional support to this alternative.

Nevertheless, this controversy remains unresolved with respect to the sensation of pruritus. As mentioned above, each cutaneous modality can be represented by a specific type of receptor, with the exception of itch. Recently a search of all types of receptors in cat hairy skin for those responsive to an itch-producing agent (cowhage) revealed that only polymodal nociceptors could be activated [22]. However, polymodal neurons also respond to other types of noxious stimuli and are currently thought to signal pain [20,23]. Since itch and pain are separate sensory modalities [24,25], the general debate between specificity and the patterning of somatosensory information can be focused on the possibility that itch and pain share a common sensory apparatus [25–29] and consequently that different patterns of activity are required for the central nervous system to differentiate between itch and pain.

A direct test of the pattern hypothesis is to determine whether artificial trains of electrical stimuli and natural stimuli evoke the same sensation. If so, this is strong evidence that a specific pattern is not required [30]. Prior observations that itch can be evoked by electrical stimulation of hairy skin in humans [31–34] suggested a test of the possibility that a unique pattern of activity is required to generate pruritus. Instead it was found that electrical stimulation of the skin produced itch over a range of frequencies and patterns. Some of these results have been presented in a preliminary communication [35].

MATERIALS AND METHODS

Animal Experiments

Adult cats were anesthetized with pentobarbital and unit recordings of activity in unmyelinated fibers were obtained from strands of the sural nerve. The general experimental procedures have been described elsewhere [36]. The receptive fields of polymodal receptors were located with mechanical stimuli [37] and were identified as polymodal by their response to mechanical, thermal, and chemical stimuli [17,22]. One stimulating electrode was placed over the receptive field of a polymodal nociceptor and the other clipped to the skin near the pad of the hind foot, with saline-soaked cotton balls (2–3 mm diameter) placed between the electrodes and the skin. The stimulating current was increased until receptor activation continued for 30 sec at a 10-Hz stimulation rate. The receptor was then stimulated at 2, 4, 10, 20, and 40 Hz with square-wave pulses 7 msec in duration. The receptor responses were recorded on analog tape and the average number of impulses per sec, over a 5-sec period, was calculated from the tracing reproduced by a light beam recorder.

In other experiments the skin over 3 polymodal receptors was heated with a Peltier cell at 0.07°C/sec from an initial temperature of 40°C to a final temperature of 48–50°C and held at this temperature for about 20 sec. The response of the receptor was recorded on magnetic tape. Temperature was monitored with a thermistor placed between the stimulator and the skin. After a 10–15 min wait the receptor's response to cowhage was also recorded. For 2 polymodal receptors the procedure was reversed, with cowhage application preceding the heat stimulus. Each response was separately transcribed on cassette tapes that were labeled without the experimenter's knowledge.

Psychophysics

Twenty-four subjects (13 male, 11 female) were electrically stimulated through saline-soaked, 3 × 2 cm, gauze pads. Before the experiment began the nature of the procedure was fully explained and the subject's informed consent was obtained, with the understanding that the subject could drop out of the experiment at any time. Initially both pads were placed on the forearm, one on the volar aspect of the wrist and the other 15–18 cm more proximal. In later experiments one pad was kept on the wrist and the other was shifted to the ankle. Square-wave pulses, 7 msec in duration, were delivered through an optically coupled, constant-current isolation unit (Grass Instruments, PSIU6, less than 1 nA leakage current). At the beginning of the experiment the current of a 10-Hz stimulus was gradually increased until the subject felt a persistent sensation. Each subject was instructed: "I will gradually turn up the intensity of the stimulus. Describe for me the first sensation that you feel." The sensation, its location, and whether the sensation changed when the polarity of the stimulus was reversed, were recorded.

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Then pairs of stimuli were delivered. The instruction was: "Now I'm going to give you a pair of stimuli. One stimulus will remain exactly the same throughout the test and I will call it the control. The other stimulus will be varied and I will call it the comparison. What I want you to do is compare the intensity of the comparison to the control. For example, you might report that the comparison is 25% greater than, equal to, or 25% less than the control. I will repeat the stimulus pair, if you wish, before you make a judgement. Report any changes in the quality of the sensation evoked by the different stimulus pairs." Subjects had no visual or auditory clues as to which stimulus pair was to be presented. The duration of each stimulus was 5 sec with a 10-sec wait between stimuli within a pair, and the subjects were told when each stimulus was turned on and off. The time between pairs varied depending on how long the subject took to decide on the relative strength of the 2 stimuli but was a minimum of 20 sec. The control stimulus was 10 Hz and the test stimuli had frequencies of 2, 4, 10, 20, 40, or 100 Hz. (Preliminary experiments indicated that below 2 Hz most subjects did not perceive any sensation.) To check for ordering effects, each frequency combination was given with the control first and also with the control last, for a total of 12 pairs delivered at random. For 5 subjects the series was repeated after 4–6 weeks. Although subjects were allowed to repeat a stimulus pair, only a few asked to do so.

Experiments were performed in a quiet room with only the subject and experimenter present. The noises produced when the stimulus frequency was changed gave no information to the subject as to which stimulus would be presented next and the stimulator was out of view of the subject. There was no sensation of air movement in the room and the relative humidity was about 45%. Skin temperature was not monitored.

After the electrical stimulation was completed, each subject was stimulated with cowhage, *Mucuna pruriens* [38]. Before cowhage was applied, the subject was told: "I am going to press some cowhage spicules into your skin. I want you to tell me when you first feel any sensation and then describe the sensation that develops. Try to compare this sensation with that from the electrical stimulation." Under magnification (6×), a bunch of cowhage spicules (approximately 10–20) was pulled from a pod using jeweler's forceps and inserted in the skin of the wrist that had not been electrically stimulated. The latency to first sensation was timed, and the spicules were removed after this sensation had reached a constant intensity.

In separate experiments recordings of the response of cat polymodal nociceptors to pruritic and pain-producing stimuli were used to stimulate subjects in a double-blind procedure (see above). Subjects were stimulated with pulses (7 msec duration) through 3 × 2 cm gauze pads attached to the wrist and ankle and asked to report any differences in the sensations evoked by the recorded responses.

Tests were made of whether the sensation of touch could be evoked with electrical stimulation of the skin. To elicit touch sensations on hairy skin it was necessary to use pulses of short duration. A pair of saline-moistened stainless steel electrodes (16 × 16 mm, about 4 cm apart) were placed on the forearm. With the stimulator set to its minimum pulse width and maximum current (2-Hz rate), the pulse width was gradually lengthened until the subject reported a sensation. With the pulse width held constant at this value, the stimulus frequency was increased from 2 to 40 Hz and the subject again asked to report his threshold sensations as the current was gradually increased from zero. To elicit touch on glabrous skin, the thumb was stimulated through one gauze pad with the other pad placed on the ankle. With pulses (7 msec duration, 10 Hz) the current was gradually increased until a threshold sensation was experienced. Then hairy skin near the wrist was tested and the evoked sensations were compared. In some experiments with the electrode on the thumb, the current was gradually increased to noxious levels and the quality of the sensation described.

Other experiments investigated conditions under which the threshold sensations evoked by electrical stimulation of hairy skin might become painful. With negative polarity on the gauze ankle electrode, the wrist was stimulated through a wire touching a drop of electrode paste about 1–2 mm in diameter (Redux Creme, Hewlett Packard). Then the wrist electrode was exchanged for a small cotton ball, 1–2 mm diameter, soaked in saline. In some cases a wisp of cotton was pulled away from the cotton ball and allowed to contact the skin, reducing the stimulated area.

All subjects reported that they had had no history of itching dermatitis. Two subjects said that their skin was sensitive to mechanical stimulation and developed wheal-and-flare reactions following firm mechanical rubbing. Upon exposure to electrical and cowhage stimuli, they did not develop reactions larger than the other subjects and their descriptions of the evoked sensations were similar to the other subjects.

For regression analysis the data were transformed using various scaling procedures (such as log transformation). Least squares regression lines were determined as was the variance of the sampled data with respect to each regression line. The regression with least variance was considered to best represent the data (F-test). With the exception of tests for regression and for homogeneity of variances (Bartlett's test), all tests were nonparametric, and all tests were two-tailed.

RESULTS

Response of Polymodal Nociceptors to Electrical Stimuli

It is possible that itch and pain are signaled by different patterns of activity along a single sensory channel (see above). Since pruritus can be evoked by electrocutaneous stimulation [31–34], it was of interest to determine how receptors that respond to itch-producing substances would react to electrical stimulation of their receptive fields.

The receptive fields of 18 polymodal receptors were stimulated electrically and 6 survived long enough for the entire protocol of electrical stimuli and cowhage application to be completed (see Materials and Methods). One did not respond to cowhage. Fig 1 shows the responses of the other 5 polymodal neurons (in 4 cats) to electrical stimulation at different rates. Through 10 Hz, all but 1 neuron were able to follow the stimulation rate. Three of the 5 neurons fatigued between the 10- and 20-Hz stimulation rates and all but 1 fatigued above 20 Hz. The average response of the population remained constant, about 10 impulses (imp)/sec, between 10- and 40-Hz rates of stimulation. For all trials (N = 50) the neural activity ended abruptly with the cessation of the electrical stimulus.

Fig 1 shows that for 2 receptors the 2-Hz stimulation rate produced an average number of impulses that was greater than 2 imp/sec. For 1 receptor, spontaneous activity was occurring before the electrical stimulation began and hence the added discharge was probably due to sensitization [17]. In the other receptor, doublets were generated by the electrical pulse. The action potentials were consistently spaced 12 msec apart, were not generated at higher rates of stimulation, and did not reappear at the 2-Hz stimulation rate following higher rates of stimulation. (Another receptor not tested with cowhage produced a doublet that persisted as the duration of the electrical pulse was decreased from 7 to 0.5 msec.) The distribution of

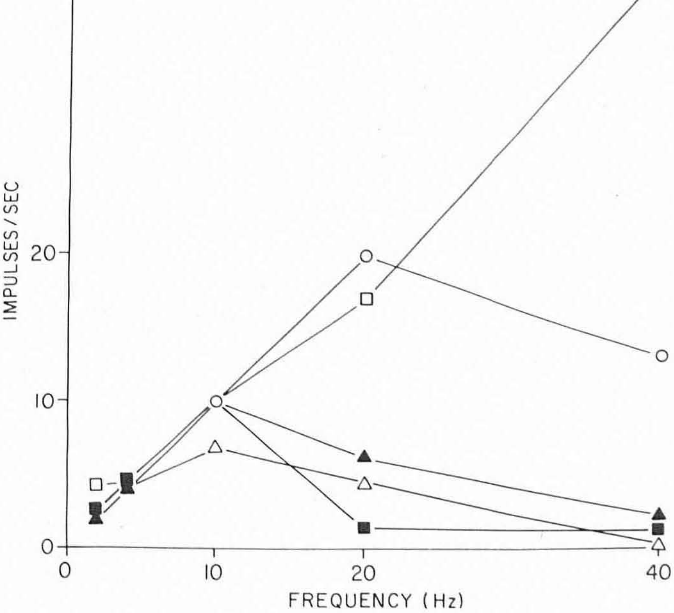

FIG 1. Ability of polymodal nociceptive neurons to follow different frequencies of cutaneous stimulation. Note that all but one neuron began to fatigue at stimulus rates between 10 and 20 Hz.

interspike intervals for the first 5 min of this receptor's response to cowhage showed that of the total number of action potentials (N = 190), only 1 had an interspike interval of 15 msec or less and 4 had intervals of 40 msec or less. In conclusion, although the mechanism of doublet formation is unknown, it appears unlikely that the doublet frequency signals the sensation of itch.

Response of Human Subjects to Patterns of Electrical Stimuli

One means by which both itch and pain could be transmitted by the same receptor population is for different patterns of activity to be generated by the two types of stimuli. Natural patterns of activity were recorded from polymodal receptors while they were responding first to a pain-producing stimulus and then to an itch-producing substance. It was then determined whether the different patterns of activity would evoke different sensory qualities in human subjects.

Recordings were made of the responses of 3 polymodal nociceptors to noxious heat [median (M) discharge rate = 3.2 imp/sec, maximum rate (MR) = 45.0 imp/sec), and cowhage (M = 3.5 imp/sec, MR = 38.0 imp/sec)]. These recordings were used to stimulate human subjects in randomized, double-blind experiments. The subjects (N = 4) did not sense any difference in the quality of the pruritic sensation for the two types of recorded responses.

It was possible that heating the skin to noxious levels altered the discharge patterns of these receptors to the subsequent cowhage stimulus. The skin of human subjects (N = 3) was heated as with the experimental animals and 10 min later cowhage applied to the stimulated area. Two subjects reported no itching. Although the inhibition of pruritus might be due to a central mechanism (see Discussion), the experiment described above was repeated with cowhage applied to polymodal receptors first, and then heat (N = 2). As before, the subjects (N = 3) felt itch on all trials.

In summary, when the discharge pattern from polymodal receptors activated by pain- and itch-producing stimuli was used to electrically stimulate human subjects, they felt the sensation of itch independent of the order with which the stimuli were applied to the receptors.

Response of Human Subjects to Steady Rates of Electrical Stimulation

If a specific pattern of discharge were necessary to signal pruritus, it is unlikely to be a regular train of impulses since to my knowledge polymodal nociceptors do not fire at steady rates (unpublished observations; [17]). Hence, if itch could be produced with a regular train of stimuli, this would be good evidence that a specific pattern is not required to generate pruritus [30].

As a subject's skin was electrically stimulated at 10 Hz, the current was gradually increased until a sensation was produced that was strong enough to be easily perceived and stable over a period of about 30 sec. The subject was then asked to describe the sensation. Twenty-two of the 24 subjects (92%) reported a sensation of itch, and all who reported itch felt inclined to scratch the stimulated area after the experiment. For half of the subjects the itch persisted after the experiment for time intervals varying from 5 sec up to 10 min.

The sensations reported can be divided into 3 general categories. (1) Twelve subjects (50%) developed only pruritus. In some instances the quality of the itch was described as being stinging, burning, or pricking. (2) Ten subjects (42%) felt a mixture of itch plus one or more other distinct sensations. Some sensations possessed a nonthreatening quality such as thumping, vibrating, pressure, or tingling while others were more nociceptive, such as stinging, burning, or pricking. (A pricking itch was distinguishable from pricking plus itch because the prick and itch could be spatially separated on the surface of the skin.) In all but 1 case the predominant sensation was itch. (In this case, the subject reported an acid-burning sensation with a slight itch component.) (3) Two subjects (8%) felt, not itching, but a stinging, tingling, or burning sensation.

Response of Human Subjects to Changes in the Frequency of Stimulation

Another possibility is that the central nervous system differentiates itch from pain by the firing frequency of the polymodal population; for instance, high frequencies might signal pain and low frequencies pruritus, or vice versa. To test this alternative, subjects were stimulated electrically over a range of frequencies and asked to rate the intensity and to report any changes in the quality of evoked sensations.

Subjects were asked to judge the intensity of a test stimulus relative to a 10-Hz control. Fig 2 plots the ratio of the test-to-control intensities over a range of frequencies. There was a clear increase in intensity as the frequency increased. Below 10 Hz the ratio of intensities was less than 1, and above 10 Hz (through 40 Hz) the ratio was greater than 1. This trend was exhibited by each subject; they all rated the intensity of the stimulus greater at 40 than 2 Hz. However, the trend did not extend to the 100-Hz rate where 5 subjects (20%) reported no sensation on at least one trial and 2 subjects (8%) reported a different quality of sensation. There was a significant tendency for the intensity of itch to be less at 100 Hz than at 10, 20, or 40 Hz (Mann-Whitney test, $p < 0.001$). This reduction was likely due to fatigue of the afferent neurons at high stimulation rates (Fig 1). In addition, although the variance of the responses did not vary over the 2–40 Hz range (Bartlet's test, $p > 0.1$), it did vary over the 2–100 Hz range ($p < 0.01$), indicating that responses to 100 Hz were significantly more variable than at lower frequencies.

Fig 2 shows the linear regression of intensity of sensation vs. the log of the frequency over the 2–40 Hz range. The slope of the line was significantly greater than zero ($p < 0.001$), and an analysis of variance showed the change in reported intensity to be significant (Kruskal-Wallis, H = 185, $p < 0.001$). The variance of this regression line with respect to the intensity data was less than the variance for regression using linear frequency or interstimulus interval scaling vs. intensity and was significantly less than the variance using a log-log regression (F-test, $p < 0.01$). Such deviations from linearity in log-log coordinates have been observed for other types of psychophysical functions, especially when the intensity of the stimulus is near threshold [39].

There was no significant difference in the relative intensity of the test stimulus that was dependent on whether the control stimulus was first or second in the pair (Wilcoxian, $p > 0.1$). In addition, with both the test and control frequencies equal to 10 Hz, the ratio of intensities did not differ significantly from 1.0 (binomial test).

As reported above, 42% of the subjects reported a complex

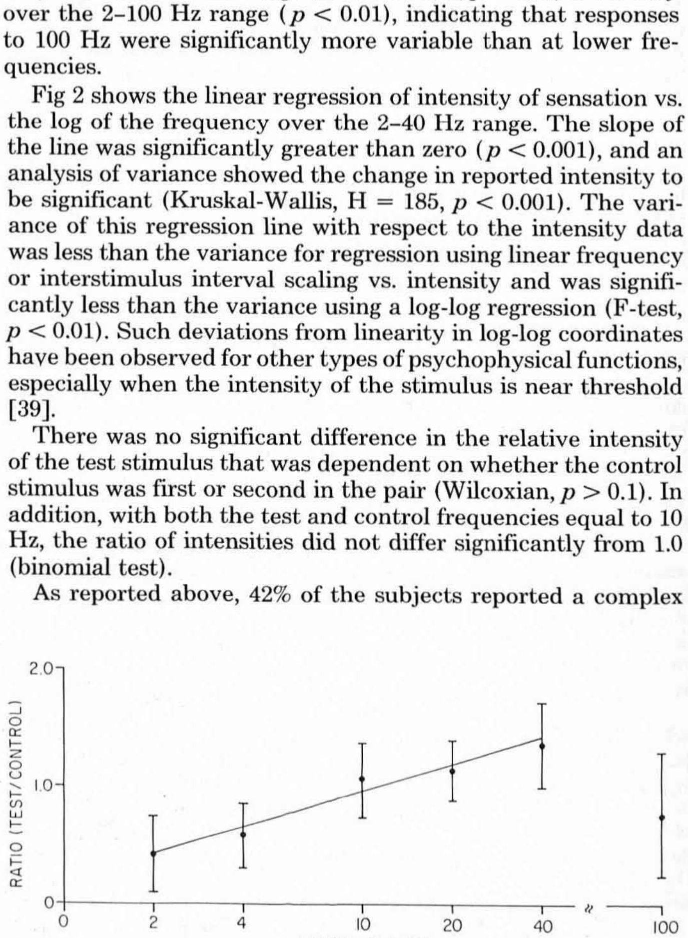

FIG 2. The intensity of sensation evoked by electrical stimulation of the skin over a range of frequencies (log scale). Slope of the regression line is 0.323; intercept is 0.197. N = 290. *Bars* indicate standard deviation.

sensation when their skin was stimulated electrically. Those who felt an itch component were asked to focus on the pruritic sensation when making the intensity discriminations shown in Fig 2. (Those who did not feel itch were asked to focus on the noxious quality of the sensation.) However, it was possible that these subjects were actually cuing on another aspect of the sensation that was also a function of stimulus frequency. An obvious component that could be used was the "pulsing," mechanical type of sensation that some subjects felt with both electrodes placed on the forearm. Since the frequency of thumping varied with the stimulus frequency, it could easily have been used as a cue. To investigate this possibility these subjects were retested with 1 of the forearm electrodes moved to the ankle, which eliminated the mechanical component of the sensation. (In some cases the mechanical sensation was referred to the hand and probably was the result of peripheral nerve stimulation.) The slopes of the regression line for intensity vs. stimulation rate for the 2 electrode placements were compared and found not to differ significantly ($p > 0.4$). It was concluded that cuing on some other aspect of the sensation besides pruritus was probably not the cause of the relationship between frequency and intensity of the pruritic sensation.

Response to Cowhage

All subjects described an itching component [40]. Twenty-one subjects (88%) said that the itch sensation from cowhage was very similar to that from electrical stimulation. Their verbal descriptions of the qualities of the sensations in the two experiences were also quite similar. The remainder (12%) reported the quality of itching to be different for the two types of stimuli.

Two subjects developed itching in response to electrical stimulation only after the experiment had been in progress for several minutes. Each experienced delayed pruritus following the application of cowhage that was preceded by the same sensory quality (pain) as had been felt at the beginning of electrical stimulation. Another subject who did not feel itch from electrical stimulation also felt the same nonpruritic (burning) sensation when cowhage was applied, with itch beginning only after 150 sec.

The latency from application of cowhage to first sensation is shown in Fig 3. To my knowledge, latency histograms have not been published by previous investigators; however, their reports of mean latencies and ranges are consistent with the data in Fig 3 [38,40,41]. After histamine is punctured into the skin, latency to pruritus is reported to be 20–30 sec [42,43] and on the blister base from 20–75 sec [24]. The mean latency to kallikrein and bradykinin is also in the 20–30 sec range [43].

DISCUSSION

A systematic search of the receptors in cat hairy skin has shown only the polymodal nociceptor to be activated by cowhage [22]. There is good evidence from peripheral nerve stimulation that activation of unmyelinated cutaneous afferent fibers can produce intense pain in human subjects [9], and it is likely that the polymodal nociceptor population transmits this sensation [20,23,30]. Hence, the question arises as to how a single afferent population might signal both pain and itch.

One possibility is that the same neuron produces a different pattern of firing for each type of stimulus that is applied, which is interpreted as pain or itch by the central nervous system. As reported above, human subjects did not perceive differences in the quality of sensation evoked by electrical stimulation of their skin with patterns of activity that were obtained from cat polymodal neurons that had been stimulated with pain-producing or pruritogenic stimuli. In other experiments subjects felt pruritus when stimulated with a regular train of pulses. Since a regular series of stimuli is itself an abnormal pattern, this result is strong evidence that a specific pattern of activity is not necessary to evoke pruritus [30]. Moveover, most subjects (N = 22) did not report any differences in the quality of itch evoked over a range of stimulus frequencies. The 2 subjects who felt the 100-Hz stimulus to have a different quality had difficulty in describing the change, but neither felt it to be more painful than the other stimuli. Instead of an alteration in quality there was an increase in the intensity of itch with increased stimulus rate. This finding is consistent with the recent observations of Torebjork and Ochoa [44] on awake human subjects. Using microelectrodes they located the receptive fields of polymodal neurons, passed current through the microelectrode, and evoked a sensation of either itch or pain that was of the same quality as that produced by stimulation of the receptive field. Changes in the frequency of stimulation did not transform pain to itch or vice versa.

An alternative mechanism for transmission of pruritus is that the polymodal population contains two subsets [45]: activation of one signals itch and the other signals pain. This possibility is consistent with the findings in the present experiments as well as those of Torebjork and Ochoa [44] (see above).

Comparison of Receptor and Human Responses to Electrical Stimulation

In response to electrocutaneous stimulation, most polymodal neurons began to fatigue at frequencies between 10 and 20 Hz (Fig 1) and their average response remained constant between 10 and 40 Hz. In contrast, human subjects continued to perceive increased intensity of sensation with stimulation rates through 40 Hz (Fig 2). It is possible that the increased pruritus at higher frequencies is signaled by a few neurons that can follow higher frequencies of stimulation (Fig 1).

Half of the subjects perceived the itch to continue for up to several minutes after the electrical stimulation had ended [31]. The absence of afterdischarge following electrical stimulation of cat polymodal receptors suggests that this aftersensation is due to activity within the central nervous system [44].

Sensations Elicited by Electrical Stimulation

When the current of 10-Hz, 7-msec duration pulses was gradually increased on the hairy skin of human subjects to levels adequate to elicit a persistent sensation, itching was the most reproducible and intense sensory quality described. This is consistent with earlier investigations [31,33,34]. On the other hand, a number of studies reported sensations of pain or touch to result from electrical stimulation. Some of these differences are probably due to the type of skin being stimulated.

Hairy skin. There are reports that under proper conditions, touch sensations such as thumping, vibration, and pulsing can be elicited by electrical stimulation of hairy skin [32, 46–50]. In one set of experiments an electrode pair was placed on the forearm and the pulse width gradually increased from its minimum width until the subject reported a sensation (see Materials and Methods). The pulse rate was held at 2 Hz. All 6 subjects tested described a tapping sensation under the electrodes at a median pulse width of 0.03 msec. With the pulse width held constant, nonpruritic sensations were felt when the stimulus frequency was increased to 40 Hz. Touch sensations are probably produced at short pulse durations because large myelinated nerve fibers are preferentially activated at short pulse widths [51]. The change in quality of evoked sensation with

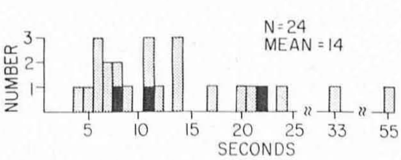

FIG 3. Latency of first reported sensation following cowhage application. For 21 subjects the first sensation was itch that gradually increased in intensity. Three others initially felt stinging or burning (latency shown as *solid bar*) and itch after 29–210 sec delay (mean = 133 sec).

pulse width substantiates the findings of others that touch sensations can be produced on hairy skin only over a restricted range of stimulus parameters [47,48,52,53].

Glabrous skin. In contrast with hairy skin, the threshold sensations on glabrous skin are touch instead of pruritus [54,47]. Even with wide pulse widths (7 msec) 5 subjects reported thumping when their thumbs were stimulated at 10 Hz and a more vibratory sensation as the frequency was gradually increased to 100 Hz. Pruritus-signaling neurons are present in glabrous skin since subjects (N = 6) felt itching after cowhage application to their thumb. It is likely that the differences in the passive properties of glabrous and hairy skin could account for the differences in response to electrical stimulation. For instance, in hairy skin the nerve terminals of itch-signaling neurons are probably quite close to the skin's surface. (Threshold current levels for pruritus in hairy skin are very low, about 15 μA [34]; also see [33,24].) Since the current density is probably greater near the skin surface, these terminals are likely to be activated at lower current levels than mechanosensitive neurons that terminate deeper in the dermis. In contrast, on glabrous skin, due to its thickess, the terminals of itch-signaling neurons might be located sufficiently deep that the profile of current density no longer differs significantly between mechanosensitive and itch terminals. As a result, myelinated neurons signaling tactile sensibility would likely be activated at lower current densities than unmyelinated neurons [9].

It is possible that at greater current strengths the sensations evoked from glabrous skin could change from touch to pruritus. However, when the current was gradually increased (thumb in 5 subjects) above that which produced touch qualities, pain was felt instead of pruritus [55–57]. These differences in sensation between glabrous and hairy skin could be due to differences in skin structure. As discussed above, at low current densities large myelinated fibers might be activated without stimulating the unmyelinated neurons that signal pruritus. Similarly, at higher levels of current the small myelinated neurons that signal pain might be stimulated without activating unmyelinated axons [9].

Pain Elicited by Electrical Stimulation of Hairy Skin

A survey of the literature indicates that painful sensations have more often been reported to result from electrical stimulation of hairy skin than pruritus (e.g., [46,48,58–61]). This could be due to a combination of factors. (1) The sensation evoked by electrical stimulation is clearly aversive; and since itch is an unpleasant sensation, it would be easy to cluster the total sensory experience as painful. (2) In some experimental paradigms the maximum currents used were higher than those in the present experiments [59,61,62]. In such cases, it is likely that the sensation was more painful than pruritic because painful stimuli, induced electrically or otherwise, can inhibit itch for several hours [42]; also see [41,63]. (3) In some cases the experimenter asked the subject to report when the evoked sensations became unpleasant, uncomfortable, or painful (e.g., [60,64,65]). Such experiments were probably not designed to investigate whether the noxious sensation contained a component of pruritus. (4) The type of conductive medium that was used might also influence the type of sensation elicited. One extensive study ([60]; also see [66]) used an electrode paste (type of paste was not reported). With paste used as a conductive medium on 6 subjects (see Materials and Methods), half reported a sensation that felt painful, similar to an acid burn, but with saline they felt itch. This result suggests that the sensation evoked might depend to some extent on the type of ions that are being iontophoretically injected into the skin. In the present experiments which used saline as a conductive medium there was no consistent relationship between the polarity of the electrodes and the sensation evoked. Subjects felt itch either under the positive or negative electrode or both, suggesting that ions other than sodium or chloride caused the painful sensations. (5) Changes in the electrode size might alter the quality of sensation from itch to pain [52]. When 6 subjects were stimulated through a small, saline-soaked pad, they all reported the pruritus to be the same as that evoked by larger electrodes (see Materials and Methods). Shelley and Arthur [33] and Bishop [31] have also reported that itch can be elicited with small electrodes. Hence this possibility seems unlikely.

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The Harvard Medical School, Department of Dermatology, will sponsor a *Conference of Specialty Clinics* at the Mount Washington Hotel, Bretton Woods, N. H., August 21–27, 1983. Further details of the unique format of this conference may be obtained from M. M. Bradley, Coordinator, Department of Dermatology, Massachusetts General Hospital, Boston, Massachusetts 02114.

At the IVe Congrès de Recherche Dermatologique (Toulouse, September 30–October 2, 1982) the creation of the *Société de Recherche Dermatologique* was announced. The object of the Society is the promotion of scientific research of the skin and skin diseases. While the Society addresses mainly researchers in French-speaking countries, one of its aims is to foster international exchange and collaboration. Interested persons are invited to contact: D. Schmitt, Secretary, Clinique Dermatologique (Pavillon R), Hôpital Edouard Herriot, 69374 Lyon, Cédex 2, France.
